

## CASE REPORT

## Adenoid cystic carcinoma: An unusual presentation

M Pushpanjali, D Naga Sujata, S Bala Subramanyam, M Jyothsna<sup>1</sup>

Department of Oral and Maxillofacial Surgery, <sup>1</sup>Department of Oral Pathology, Government Dental College and Hospital, Rajiv Gandhi Institute of Medical Sciences, Kadapa, Andhra Pradesh, India

### Address for correspondence:

Dr. D. Naga Sujata,  
Department of Oral and Maxillofacial Surgery,  
Government Dental College and Hospital,  
Rajiv Gandhi Institute of Medical Sciences,  
Kadapa - 523 001, Andhra Pradesh, India.  
E-mail: sujatamds@gmail.com

Received: 09-02-2013

Accepted: 09-07-2014

### ABSTRACT

The adenoid cystic carcinoma is a relatively rare epithelial tumor of the major and minor salivary glands, accounting for about 1% of all malignant tumor of the oral and maxillofacial regions. Peak incidence occurs between the 5<sup>th</sup> and 6<sup>th</sup> decades of life. The clinical and pathological findings typical of this tumor include slow growth, peri-neural invasion, multiple local recurrences and distant metastasis. Herein, we report a case of adenoid cystic carcinoma of oropharynx with unusual clinical presentation. The diagnosis of this case and importance of cytology in diagnosing such cases is discussed.

**Key words:** Adenoid cystic carcinoma, cribriform pattern, salivary gland malignancy

### INTRODUCTION

Adenoid cystic carcinoma (ACC) is a malignant neoplasm arising from salivary glands of head and neck region. This type of neoplasm was first described by Billroth in 1856 as a benign neoplasm and was named cylindroma for cribriform appearance formed by tumor cells with cylindrical pseudo spaces.<sup>[1]</sup> Approximately 10-15% of salivary gland tumors are ACCs.<sup>[2]</sup> ACC most often occurs in minor salivary glands and the submandibular gland and less frequently, in the sublingual and parotid glands.<sup>[3,4]</sup> Other rare locations include the aerodigestive tract, lacrimal glands and adnexal skin glands. Most ACC patients are in their fifth and sixth decade of life and females are slightly more affected than males.<sup>[2-4]</sup> ACC is a rare tumor of the head and neck. It accounts for less than 1% of all head and neck malignancies. However, it is the most common malignant tumor of the minor salivary glands (Spiro *et al.* 1979),<sup>[5]</sup> the palate being the commonest site. Less common sites where this tumor may be encountered are vulva (Abell 1963),<sup>[6]</sup> cervix (Gallager *et al.* 1971),<sup>[7]</sup> Cowper's glands (Carpenter and Bernardo 1971),<sup>[8]</sup> esophagus (Nelms and Luna 1972),<sup>[9]</sup> external auditory canal (Ramadas 1963),<sup>[10]</sup> middle ear (Baruah 1977)<sup>[11]</sup> and nasopharynx (Iqbal and Gurmurthy 1991).<sup>[12]</sup> Rarely, it may also present as primary intraosseous tumors of the mandible and maxilla (Bradley 1968, Dhawan *et al.* 1970).<sup>[13]</sup>

ACC is believed to arise from mucous-secreting glands. It arises specifically from the intercalated ducts and electronmicroscopy shows that it arises from cells that can differentiate into epithelial and myoepithelial cells. These mucus-secreting tumors are confined to structures derived from the foregut (that is, the parotid, submandibular and sublingual glands and the mucus glands throughout the upper respiratory tract). These glands are also associated with the larynx (supraglottis and subglottis), nasopharynx and oropharynx (tonsil and posterior tongue).<sup>[14]</sup>

ACC is an indolent tumor but grows relentlessly. It is typically unencapsulated. The tumor extends well beyond the visible and palpable limits of the salivary gland region. This infiltrative capacity is the hallmark of this carcinoma because of which multiple local recurrences are common despite aggressive surgical and irradiation therapy. The proliferating cell is a small cuboidal cell with a round hyperchromatic nucleus and scant cytoplasm. Mitotic activity, pleomorphism and cellular atypia are not usually seen. Histologically, three different patterns have been identified cribriform, tubular and solid types. These patterns may coexist in the same tumor but one pattern usually predominates. This is of clinical significance since predominantly solid ACC are found to be more aggressive and are associated with a worse prognosis than predominantly tubular or cribriform ACC.

ACC occasionally invades regional lymph nodes by direct extension, but true embolic lymph node metastasis is rare.<sup>[15]</sup> However, distant metastasis to organs other than lymph nodes is common, particularly late in the course of the disease, the lungs being the primary site followed by bones, the liver and the brain.<sup>[16]</sup> It is a malignancy that reinforces the point that

### Access this article online

#### Quick Response Code:



Website:  
www.jomfp.in

DOI:  
10.4103/0973-029X.140796

tumor growth rate and metastatic capability are independent tumor properties.

Clinical features depend on the site involved and the nerve affected. In nasopharyngeal localization, the symptoms most commonly found are epistaxis, progressive nasal stenosis, dysfunction of the Eustachian tube and in relation to the invasion of the skull base, disorders of ocular motility, diplopia, facial pain, dysfunction of IX, X, XI and XII pairs of cranial nerves and more rarely, Horner's syndrome. Wherever it arises, ACC presents as a painful or a painless solid tumor mass with or without ulceration, cranial nerve palsy or paresis. The present case is unusual because of its atypical clinical presentation. This case highlights the fact that ACC may rarely have clinical and radiological features similar to that of a cyst.

### CASE REPORT

A 50-year-old female reported to the Department of Oral and Maxillofacial surgery with the chief complaint of progressive dysphagia due to a swelling in relation to right oropharyngeal region. The swelling was slow growing and persistent since one year. Patient's past medical history was unremarkable and personal history was negative for tobacco consumption. No obvious neck swelling was evident. Intraoral examination revealed a 4 × 4 cm swelling in relation to right oropharynx extending superiorly from soft palate inferiorly up to palatine tonsil medially till midline displacing uvula to the left side [Figure 1]. Swelling was well-defined, soft, fluctuant, cystic in consistency, non-tender, non-pulsatile and was not fixed to the underlying tissues. The overlying mucosa was intact with no signs and symptoms of inflammation. Regional lymphadenopathy was not present. Radiographic investigations were not suggestive of any apparent pathology involving bone or dentition.

Computed tomography (CT) scan revealed a well-defined hypodense cystic mass with peripheral enhancement in relation to right parapharyngeal space. Axial CT section was showing lesion extending laterally into the masticator space medially displacing the lateral wall of oropharynx with absence of bone destruction [Figure 2]. Sagittal section revealed that the mass was extending superiorly from nasopharynx and inferiorly to the level of hyoid bone [Figure 3]. Contrast CT neck showed no evidence of involvement of lymph nodes. On Doppler, high vascular flow was not noted and thus, the possibility of low-flow lesion was suspected.

Fine needle aspiration revealed a clear amber-colored fluid and about 20 ml was aspirated at a time [Figure 4]. Smear showed sparse cellular material in a fluid-filled background. Macrophages and squamous cells with no features of dysplasia were seen. FNAC and CT scan was suggestive of a benign cystic lesion. A differential diagnosis of retention cyst and brachial cleft cyst was considered.

Incisional biopsy was performed, which revealed cribriform pattern with uniform basaloid tumor cells with scant cytoplasm and basophilic angulated nucleus, arranged in nests and islands containing circular or ovoid cystic spaces giving Swiss cheese appearance. Cystic spaces were filled with eosinophilic material [Figure 5a]. Tumor cells arranged in



Figure 1: Intra oral photograph showing extension of the swelling

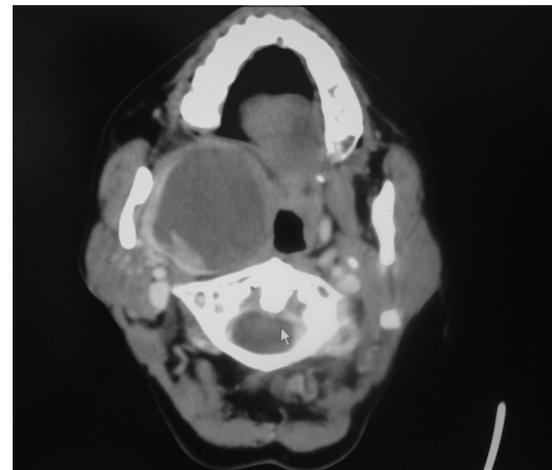


Figure 2: Axial CT section showing well defined hypodense cystic mass in right parapharyngeal space

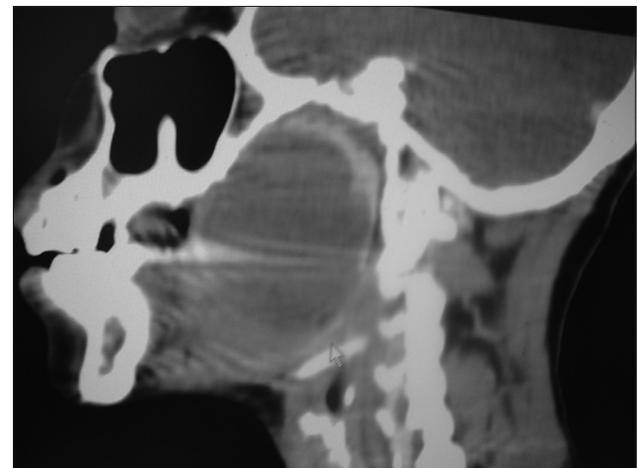


Figure 3: Sagittal CT section showing the lesion extending superiorly from nasopharynx inferiorly up to hyoid bone

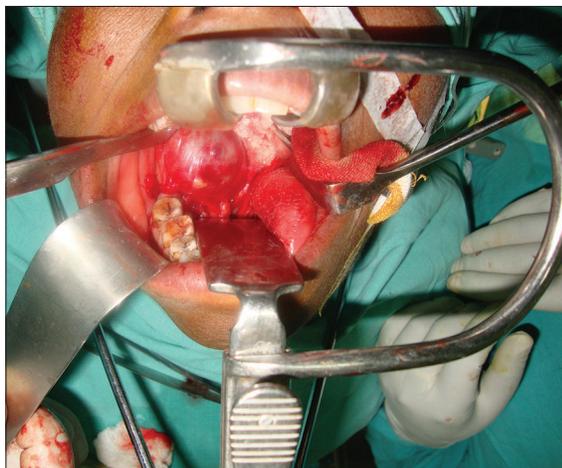
solid nests and islands without cystic spaces were also found in focal areas [Figure 5b]. Tumor islands were surrounded by hyalinized stroma. Overall histopathological picture was suggestive of cribriform type of ACC.

Total body scan performed was negative for distant metastases. Surgical excision of mass was performed through transoral route under general anesthesia. We preferred transoral approach than transcervical approach as the mass was in prestyloid region and was more prominent intraorally. The Boyle Davis mouth gag was used for better access. Intraoperatively mass was mimicking a cyst [Figure 6]. On gross examination of specimen, the surface was smooth and on palpation, was rubbery in consistency. Specimen showed thick capsule with some appreciable solid portion.

Postoperative course was uneventful. The final diagnosis of the surgical specimen was ACC. Postoperative radiation therapy was selected as supplemental treatment and patient remains disease free after 1 year 6 months [Figure 7].



**Figure 4:** Photograph showing amber-colored fluid on aspiration



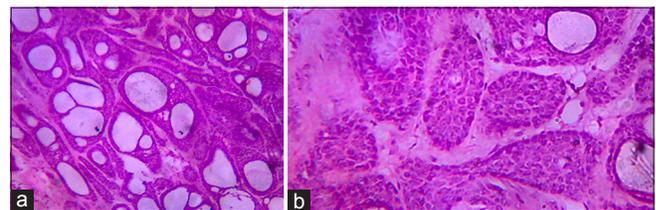
**Figure 6:** Intraoperative photograph showing tumor mass mimicking a cystic lesion

## DISCUSSION

ACC is a rare epithelial tumor with an indolent but persistent growth pattern. ACC occurs predominantly in fourth to sixth decade of life with a slight female predilection.<sup>[2-4]</sup> In our case, a 50-year-old female was affected. ACC clinically is characterized as a slow-growing mass with a propensity to invade peripheral nerves with a high recurrence rate and metastases to other organs. Pain is usually a common and important associated symptom, occasionally occurring before clinical evidence of the disease. Neoplastic cell neurotropism causes pain, which was not evident in our case, suggesting no invasion of tumor cells into adjacent peripheral nerves.

The fine-needle aspiration biopsy of ACC characteristically shows small clusters or groups of basaloid tumor cells encircling the hyaline globule. Tumor cells contain small, ovoid nucleus with mild to moderate pleomorphism and hyperchromasia.<sup>[17]</sup>

Histopathologically ACC presents as three patterns—cribriform, tubular and solid. The most important and classical feature of it is the “cribriform” pattern where nests of tumor cells have a sieve-like or “Swiss cheese” configuration. A second major pattern observed in ACC is the “tubular” pattern in which elongated tubular structures with a central lumen are seen. The third pattern is the “solid” pattern where the tumor nests and islands are completely filled with basaloid tumor cells without cystic spaces. The cystic spaces



**Figure 5:** (a): Photomicrograph revealing tumor cells arranged in cribriform pattern (H&E stain, x40), (b): Photomicrograph showing solid cell nests (H&E stain, x200)



**Figure 7:** Postoperative photograph after 1 year 6 months

may contain basophilic mucinous material or eosinophilic material. Usually, the tumor islands are ultrastructurally surrounded by fibrous stroma or hyalinized stroma, which is replicated basal lamina. In most ACC, all three patterns can usually be observed, although the distribution varies greatly between different lesions. In addition, the pattern may vary in different areas of the same mass. Tumor is graded according to Szanto *et al.*—cribriform or tubular (grade I), less than 30% solid (grade II), or greater than 30% solid (grade III).<sup>[1]</sup> ACC with high-grade transformation refers to the presence of a pleomorphic mitotically active high-grade carcinoma component arising in an otherwise conventional ACC of any pattern/grade. The transformed component is typically of a purely ductal phenotype with a solid or cribriform appearance. Unlike conventional ACC, which is characterized by small, hyperchromatic, monomorphic nuclei and scant cytoplasm, transformed components show prominent nuclear size and chromatin variability. Common features include fibrocellular desmoplasia, abundant mitoses, necrosis and microcalcifications. Unique patterns in high-grade transformation include micropapillary and squamoid growth.<sup>[18]</sup>

Immunohistochemistry reveals that the luminal tumor cells are diffusely positive for cytokeratin, epithelial membrane antigen, carcino embryonic antigen and CD117 (c-Kit) indicating ductal origin and those that surround the pseudo cysts show positivity for S-100, smooth muscle actin, calponin and variable positivity for cytokeratin suggestive of myoepithelial cell differentiation.<sup>[19-21]</sup> Over expression of p53 and Ki-67 with loss of myoepithelial markers was found in high-grade tumors.<sup>[18]</sup> There is also strong reactivity for basement membrane components such as type IV collagen, laminin and heparan sulphate (perlecan).<sup>[22-24]</sup> Affinity of tumor cells to proliferate along the basement membranes is responsible for frequent invasion of tumor cells into basement membrane-rich tissues such as peripheral nerves, blood vessels and skeletal muscles. Cytogenetically, the most consistent, although not exclusive, reported alterations have been at chromosomes 6q, 9p and 17p12-13 regions.

The differential diagnosis of ACC includes tumors that also exhibit tubular and cribriform structures such as polymorphous low-grade adenocarcinoma; tumors with basaloid cellular morphology such as basal cell adenoma and basal cell adenocarcinoma; and tumors with a dual population of ductal and myoepithelial cells such as pleomorphic adenoma. Polymorphous low-grade adenocarcinoma occurs almost exclusively in the minor salivary glands and may contain overlapping histopathologic features with ACC such as ductal, tubular and even cribriform growth. Perineural invasion is also common. However, the presence of cuboidal or columnar cells containing pale and ovoid nuclei with eosinophilic cytoplasm is in contrast with the hyperchromatic and angulated cells of ACC. In addition, polymorphous low-grade adenocarcinoma shows low expression of c-KIT compared with the high c-KIT

expression of ACC. Pleomorphic adenoma can be identified by the presence of mesenchymal, especially cartilaginous differentiation in the stroma. Pleomorphic adenoma expresses glial fibrillary acidic protein and CD57, but ACCs do not react with these markers. Basal cell adenoma can be identified by the presence of a capsule and lack of stromal and perineural invasion. Basal cell adenocarcinoma may be more difficult to differentiate with solid ACC; however, lack of clear cytoplasm and hyperchromatic, angulated nuclei with the presence of peripheral palisaded nuclei in the former may aid in diagnosis.<sup>[25]</sup> Also, most tumors displaying a solid component of ACC will often display areas of cribriform or tubular growth.

Spiro *et al.*<sup>[26]</sup> found the following factors to be important in prognosis: Site, size and extension into adjacent structures. Blanck *et al.*<sup>[27]</sup> reported an increased mortality with perineural invasion and numerous mitoses. Perineural invasion and bone destruction was not present in our case, favoring good prognosis. The underlying principle in the treatment of ACC is that tumor cells extend well beyond the clinical or radiographic margins and this tumor undergoes not only perineural invasion but also perineural spread. Therefore, it generally requires excision with the widest margins possible and postoperative radiation therapy of 6000-7500 cgy.<sup>[28]</sup> The best treatment considered for ACC is unanimously radical surgical resection followed by radiotherapy. However, in cases of nasopharyngeal extension, the frequent perineural and perivascular infiltrations association with the anatomical structures of the nasopharynx make the surgical approach risky on account of technical difficulties, substantially due to the proximity of surgical margins to critical neural and vascular structures. Surgical treatment, therefore, is often characterized by incomplete excision, consequently leading to increased frequency of local recurrence.

ACCs have a well-known prognostic profile. The 5-year survival rate is 75% but 10-year survival rate is only 20% and survival rate at 15 years is about 10%. Overall prognosis relates to several factors histologically solid patterns bode worse than cribriform pattern. In our case, lesion was cribriform type, which has better prognosis. Clinical size >4 cm is indicative of more subclinical spread and is associated with a worse prognosis. Delayed diagnosis and treatment also worsens the prognosis. Surgical margins that are not clear or close, despite postoperative radiation therapy are also associated with a poor prognosis, which is the single most important factor associated with local recurrence.

## CONCLUSION

The case cited here is an example of the dilemma in diagnosis. Clinical and CT findings were suggestive of a benign cystic mass and diagnosis of ACC was not realized until pathologic sections were studied. In view of histopathologic findings, postoperative irradiation was selected as supplemental

treatment. The present case highlights the need to be aware of unusual presentation of ACC as soft, fluctuant cystic mass.

## REFERENCES

- Szanto PA, Luna MA, Tortoledo ME, White RA. Histologic grading of adenoid cystic carcinoma of the salivary glands. *Cancer* 1984;54:1062-9.
- Chummun S, McLean NR, Kelly CG, Dawes PJ, Meikle D, Fellows S, *et al.* Adenoid cystic carcinoma of the head and neck. *Br J Plast Surg* 2001;54:476-80.
- Nascimento AG, Amaral AL, Prado LA, Kligerman J, Silveira TR. Adenoid cystic carcinoma of salivary glands. A study of 61 cases with clinicopathologic correlation. *Cancer* 1986;57:312-9.
- Mendenhall WM, Morris CG, Amdur RJ, Werning JW, Hinerman RW, Villaret DB. Radiotherapy alone or combined with surgery for adenoid cystic carcinoma of the head and neck. *Head Neck* 2004;26:154-62.
- Spiro RH, Huvos AG, Strong EW. Adenoid cystic carcinoma: Factors influencing survival. *Am J Surg* 1979;138:579-83.
- Abell MR. Adenocystic (Pseudoadenomatous) basal cell carcinoma of vestibular glands of vulva. *Am J Obstet Gynaecol* 1963;86:470-82.
- Gallager HS, Simpson CB, Ayala AG. Adenoid cystic carcinoma of the uterine cervix. Report of 4 cases. *Cancer* 1971;27:1398-402.
- Carpenter AA, Bernardo JR Jr. Adenoid cystic carcinoma of Cowper's glands: Case report. *J Urol* 1971;106:701-3.
- Nelms DC, Luna MA. Primary adenoid cystic carcinoma (cylindromatous carcinoma) of the oesophagus. *Cancer* 1972;29:440-3.
- Ramadass T. Cylindroma of external ear. *J Laryngol Otol* 1966;80:863-6.
- Baruah T. Adenoid cystic carcinoma of middle ear. *Indian J Otolaryngol* 1977;29:143-4.
- Iqbal MS, Gurmurthy J. Adenoid cystic carcinoma of nasopharynx. *Indian J Otolaryngol* 1991;43:199-200.
- Dhawan IK, Bhargava S, Nayak NC, Gupta RK. Central salivary gland tumours of jaws. *Cancer* 1970;26:211-7.
- Jones AS, Hamilton JW, Rowley H, Husband D, Helliwell TR. Adenoid cystic carcinoma of the head and neck. *Clin Otolaryngol Allied Sci* 1997;22:434-43.
- Allen MS Jr, Marsh WL Jr. Lymph node involvement by direct extension in adenoid cystic carcinoma. Absence of classic embolic lymph node metastasis. *Cancer* 1976;38:2017-21.
- Locati LD, Guzzo M, Bossi P, Massone PP, Conti B, Fumagalli E, *et al.* Lung metastasectomy in adenoid cystic carcinoma (ACC) of salivary gland. *Oral Oncol* 2005;41:890-4.
- Dutta NN, Baruah R, Das L. Adenoid cystic carcinoma-Clinical presentation and cytological diagnosis. *Indian J Otolaryngol Head Neck Surg* 2002;54:62-4.
- Seethala RR, Hunt JL, Baloch ZW, Livolsi VA, Leon Barnes E. Adenoid cystic carcinoma with high-grade transformation: A report of 11 cases and a review of the literature. *Am J Surg Pathol* 2007;31:1683-94.
- Azumi N, Battifora H. The cellular composition of adenoid cystic carcinoma. An immunohistochemical study. *Cancer* 1987;60:1589-98.
- Caselitz J, Becker J, Seifert G, Weber K, Osborn M. Coexpression of keratin and vimentin filaments in adenoid cystic carcinomas of salivary glands. *Virchows Arch A Pathol Anat Histopathol* 1984;403:337-44.
- Caselitz J, Jaup T, Seifert G. Immunohistochemical detection of carcinoembryonic antigen (CEA) in parotid gland carcinomas. Analysis of 52 cases. *Virchows Arch A Pathol Anat Histol* 1981;394:49-60.
- Cheng J, Saku T, Okabe H, Furthmayr H. Basement membranes in adenoid cystic carcinoma. An immunohistochemical study. *Cancer* 1992;69:2631-40.
- Kimura S, Cheng J, Ida H, Hao N, Fujimori Y, Saku T. Perlecan (heparan sulfate proteoglycan) gene expression reflected in the characteristic histological architecture of salivary adenoid cystic carcinoma. *Virchows Arch* 2000;437:122-8.
- Loducca SV, Raitz R, Araújo NS, Araújo VC. Polymorphous low-grade adenocarcinoma and adenoid cystic carcinoma: Distinct architectural composition revealed by collagen IV, laminin and their integrin ligands (alpha2beta1 and alpha3beta1). *Histopathology* 2000;37:118-23.
- Jaso J, Malhotra R. Adenoid cystic carcinoma. *Arch Pathol Lab Med* 2011;135:511-5.
- Spiro RH, Huvos AG, Strong EW. Adenoid cystic carcinoma of salivary origin. A clinicopathologic study of 242 cases. *Am J Surg* 1974;128:512-20.
- Blanck C, Eneroth CM, Jacobsson F, Jakobsson PA. Adenoid cystic carcinoma of the parotid gland. *Acta Radiol Ther Phys Biol* 1967;6:177-96.
- Robert EM, Diane S. *Oral and Maxillofacial Pathology: A rational for diagnosis and management.* 1<sup>st</sup> ed. New Delhi: Quintessence Publishing Co, Inc; 2003. p. 550-3.

**How to cite this article:** Pushpanjali M, Sujata DN, Subramanyam SB, Jyothisna M. Adenoid cystic carcinoma: An unusual presentation. *J Oral Maxillofac Pathol* 2014;18:286-90.

**Source of Support:** Nil. **Conflict of Interest:** None declared.